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(21) International Application Number: PCT/US94/06789 (22) International Filing Date: 15 June 1994 (15.06.94) (30) Priority Data: 08/080,372 18 June 1993 (18.06.93) US (71) Applicant: POLYMER TECHNOLOGY CORPORATION [US/US]; 100 Research Drive, Wilmington, MA 01887 (US). (72) Inventors: ELLIS, Edward, J.; 9 Hampton Court, Lynnfield, MA 01940 (US). ELLIS, Jeanne, Y.; 9 Hampton Court, Lynnfield, MA 01940 (US). (74) Agents: THOMAS, John, E. et al.; Bausch & Lomb Incorporated, One Chase Square, P.O. Box 54, Rochester, NY 14601-0054 (US).		(81) Designated States: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: CONTACT LENS SOLUTION CONTAINING PEO AND CATIONIC CELLULOSE (57) Abstract Compositions for treating contact lenses comprise a cationic cellulosic polymer and polyethylene oxide.		

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CONTACT LENS SOLUTION CONTAINING PEO AND CATIONIC
CELLULOSE

BACKGROUND OF THE INVENTION

This invention relates to compositions for treating contact lenses, especially rigid, gas permeable contact lenses.

The surfaces of contact lenses must have a certain degree of hydrophilicity to be wet by tears. Tear wettability is in turn necessary to provide the lens wearer with comfort and good vision.

One way to impart wettability to contact lens surfaces is to add hydrophilic monomers to the mixture of comonomers used to form the contact lens material. However, the relative amount of hydrophilic monomer added affects physical properties other than wettability. For example, the hydrophilic monomer content of rigid gas permeable lens materials is much less than that of soft, hydrogel lenses. The rigid lenses accordingly contain only a few percent water of hydration whereas soft lenses contain amounts varying from 10 to 90 %. Thus, while hydrophilic monomer addition does increase wettability, the technique is limited by the influence that it has on other properties.

Another way to impart wettability to lens surfaces is to modify the surface after polymerization. For example, surface coatings of hydrophilic polymers have been grafted onto the surface. Plasma treatment has also been used to increase the hydrophilicity of hydrophobic surfaces. Although effective, methods such as these are often expensive (requiring complicated and difficult manufacturing procedures) and impermanent.

Water soluble polymers in lens care solutions have also been used to enhance the wettability of lens surfaces. Use of wetting polymers in this way provides a "cushion" between the lens and the eye which is equated with increased wettability as wearer comfort and tolerance. However, a common drawback with this approach is that the cushion layer dissipates rapidly, since there is little specific interaction between the polymer and the lens surface.

United States Patent Nos. 4,168,112 and 4,321,261 disclose a method to overcome this drawback by immersing the lens in a solution of an oppositely charged ionic polymer to form a thin polyelectrolyte complex on the lens surface. The complex increases the hydrophilic character of the surface for a greater period of time relative to an untreated surface. Of particular interest are cellulosic polymers bearing a cationic charge, said polymers forming a strongly adhered hydrophilic layer on the contact lens surface.

These polymers have proven to be exceptional components for wetting, soaking, and lubricating solutions.

While these cationic polymers are extremely effective for increasing the wettability of the lens, it would be desirable to enhance the biocompatibility of the complex formed by cationic cellulosic polymers to increase comfort to the eye.

Polyethylene oxide (PEO) is a unique water soluble polymer. When in an aqueous environment PEO does not perturb the structure of water and therefore is very "compatible" in a water matrix. Because of these unusual properties, PEO has been found to be an effective polymer for low protein adsorptions and low cell adhesion characteristics. However, PEO has little or no affinity for surfaces, frustrating attempts to employ PEO in solution as a biocompatibilizer. Rather, previous attempts to employ PEO as a biocompatibilizer have focused on coating PEO on polymeric surfaces, such as by grafting or covalently bonding PEO to the surfaces.

SUMMARY OF THE INVENTION

The invention provides aqueous compositions for treating contact lenses comprising a cationic cellulosic polymer and polyethylene oxide. The compositions are especially effective at increasing the

wettability of the surface of a lens treated therewith, particularly rigid, gas permeable (RGP) contact lenses.

Additionally, the invention relates to methods of treating a contact lens which employ the compositions.

DETAILED DESCRIPTION OF THE INVENTION

The invention provides aqueous compositions for treating contact lenses comprising a cationic cellulosic polymer and polyethylene oxide.

The cellulosic polymer component has a cationic charge, and the polymer should be compatible with the eye, non-irritating, and yet should form a hydrogel which is electrostatically bound to the surface of the contact lens treated with the composition.

Examples include cellulosic polymer containing N,N-dimethyl amino ethyl groups (either protonated or quaternized), and cellulosic polymers containing N,N-dimethyl amino-2-hydroxylpropyl groups (either protonated or quaternized).

Cationic cellulosic polymers are commercially available or can be prepared by methods known in the art. As an example, the quaternary nitrogen-containing cellulosic polymers can be prepared by reacting hydroxyethyl cellulose with a trimethyl ammonium substituted epoxide. Various preferred cationic cellulosic polymers are commercially available water soluble polymers available under the CTFA (Cosmetic,

Toiletry, and Fragrance Association) designation Polyquaternium-10, including the cationic cellulosic polymers available under the tradename UCARE® Polymer from Amerchol Corp., Edison, New Jersey, USA). These polymers are believed to contain quaternized N,N-dimethyl amino groups along the cellulose polymer chain.

Polyethylene oxide (PEO), also called polyethylene glycol or PEG, improves the biocompatibility of the contact lenses treated with the solution, enhancing resistance to protein absorption of the lens. PEO is commercially available under a wide variety of tradenames from various suppliers.

The cationic cellulosic polymer absorbs rapidly and strongly on the surfaces of contact lenses, particularly lenses containing anionic sites, and once absorbed, this material desorbs very slowly. In contrast, PEO absorbs very weakly, at best, on such lens surfaces. Thus, although PEO enhances biocompatibility of polymeric surfaces, the use of PEO in solution to biocompatibilize such surfaces is not particularly effective.

Applicants have found that aqueous solutions of the cationic cellulosic polymers and PEO provide unique effects when used to treat a contact lens. More specifically, some type of complexation, or "entanglement", occurs between these two materials.

Despite this complexation, the resultant complex is still able to absorb relatively strongly on the lens surface, thereby anchoring the PEO to the surface as well. The compositions enhance the wetting ability, biocompatibility, and protein deposition resistance of contact lenses treated therewith.

The cationic cellulosic polymer may be employed at about 0.001 to about 10 weight percent of the composition, more preferably at about 0.01 to about 2 weight percent. PEO may be employed at about 0.001 to about 10 weight percent of the composition, more preferably at about 0.01 to about 5 weight percent.

Typical contact lens solutions include necessary buffering agents for buffering or adjusting pH of the composition, and/or tonicity adjusting agents for adjusting the tonicity of the composition.

Representative buffering agents include: alkali metal salts such as potassium or sodium carbonates, acetates, borates, phosphates, citrates and hydroxides; and weak acids such as acetic, boric and phosphoric acids.

Representative tonicity adjusting agents include: sodium and potassium chloride, and those materials listed as buffering agents. The tonicity agents may be employed in an amount effective to adjust the osmotic value of the final composition to a desired value. Generally, the buffering agents and/or tonicity

adjusting agents may be included up to about 10 weight percent.

According to preferred embodiments, an antimicrobial agent is included in the composition in an antimicrobially effective amount, i.e., an amount which is effective to at least inhibit growth of microorganisms in the composition. Preferably, the composition can be used to disinfect a contact lens treated therewith. Various antimicrobial agents are known in the art as useful in contact lens solutions, including: chlorhexidine (1,1'-hexamethylene-bis[5-(p-chlorophenyl) biguanide]) or water soluble salts thereof, such as chlorhexidine gluconate; polyhexamethylene biguanide (PHMB, a polymer of hexamethylene biguanide, also referred to as polyaminopropyl biguanide) or water-soluble salts thereof, such as the polyhexamethylene biguanide hydrochloride available under the trade name Cosmocil CQ (ICI Americas Inc.); benzalkonium chloride; and polymeric quaternary ammonium salts. When present, the antimicrobial agent may be included at 0.00001 to about 5 weight percent, depending on the specific agent.

The compositions may further include a sequestering agent (or chelating agent) which can be present up to about 2.0 weight percent. Examples of preferred sequestering agents include ethylenediaminetetraacetic acid (EDTA) and its salts,

with the disodium salt (disodium edetate) being especially preferred.

The compositions containing the cationic cellulosic polymer and PEO are very effective at providing the compositions with the ability to wet surfaces of contact lenses treated therewith. If desired, the composition may include as necessary a supplemental wetting agent. Representative wetting agents include: nonpolymeric cellulosic materials such as hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose and methylcellulose; polyvinyl alcohol; and polyvinyl pyrrolidone. Such additives, when present, may be used in a wide range of concentrations, generally about 0.1 to about 10 weight percent.

Contact lenses are treated with the compositions by contacting the lenses with the compositions. For example, a contact lens can be stored in the solution, or soaked in the solution, for sufficient time to wet the surfaces thereof. The treated lens can be inserted directly in the eye, or alternately, the lens can be rinsed. Alternately, drops of solution can be placed on the lens surface and the treated lens inserted in the eye. The specific lens care regimen used will depend on the other compounds present in the solution, as is well known in the art.

For compositions containing an antimicrobial agent, the a contact lens is preferably soaked in the composition for sufficient time to disinfect the lens and wet the surface thereof.

The following examples illustrate various preferred embodiments of the invention.

In the Examples, dynamic contact angle measurements were made on hydrated, polished wafers of a fluorosilicone rigid gas permeable (RGP) contact lens material (BOSTON RXD®, Polymer Technology Corporation, Boston, Massachusetts) utilizing a Cahn Instruments DCA 322. Wafers were dipped in the test solution 7 times at an average rate of 225 microns per second. All tests were run at room temperature. A computer assisted mathematical analysis of the data yields a graph of contact angle plotted against the vertical position on the wafer. The average advancing and receding contact angles were obtained from the graph.

EXAMPLE 1

Solutions containing the following ingredients were prepared and passed through a 0.22 micron sterilizing filter in a clean room environment. The solutions were then packaged in sterile bottles. In the Examples, UCARE® Polymer JR-30M is a polymeric quaternary ammonium salt of hydroxyethyl cellulose reacted with a trimethyl ammonium substituted epoxide,

available from Amerchol Corp. POLYOX WSR N-10® is a polymer of ethylene oxide wherein the number of ethylene oxide units averages 2000, supplied by Union Carbide Corp., Tarrytown, New York.

Dynamic contact angles (DCA) were determined for the RGP material in various solutions described in TABLE 1. The DCA results are presented in TABLE 2. It is noted that Solution A lacked PEO and Solution D lacked a cationic cellulosic polymer. In Solution B, the ratio of cationic cellulosic polymer to PEO was 70:30, and in Solution C, this ratio was 30:70.

The dramatic lowering of the advancing contact angle with Solutions B and C indicates the presence of a polymer complex which is hydrophilic and bound to the surface.

TABLE 1Solution

	A	B	C	D
Sodium Phosphate, dibasic %	0.280	0.280	0.280	0.280
Potassium Phosphate, monobasic %	0.055	0.055	0.055	0.055
Sodium Chloride %	0.700	0.700	0.700	0.700
Potassium Chloride %	0.050	0.050	0.050	0.050
Disodium Edetate %	0.050	0.050	0.050	0.050
UCARE Polymer JR-30M %	0.090	0.063	0.027	0
POLYOX WSR N-10 %	0	0.027	0.063	0.027
Deionized Water Q.S. %	100	100	100	100

TABLE 2

Solution	A	B	C	D
Adv ϕ	78	41	40	91
Rec ϕ	37	37	35	40
Adv-Rec	41	4	5	51

Adv. = Advancing contact angle in degrees
 Rec = Receding contact angle in degrees
 Adv-Rec = Difference between advancing and receding contact angles

EXAMPLE 2

Solutions designated A1, B1, C1 and D1 were prepared as in Example 1. Each of Solutions A1, B1, C1 and D1 corresponded to Solutions A, B, C and D,

12

respectively, except that the solutions further included 15 ppm polyhexamethylene biguanide.

Solutions A1, B1, C1 and D1 were evaluated on eye to assess clinical performance. Clean BOSTON RXD lenses for adapted RGP lens wearers were soaked in the solutions overnight. Each subject installed the lenses directly from the solution (no rinse step) and was examined immediately by a clinician who evaluated a number of parameters using a biomicroscope. The compiled results of the clinical evaluation of solutions A1 through D1 are presented below.

	TBUT*	Wetting	Tear Film
A1	10	100% Surface	Occasional Thin Spots
B1	11	100% Surface	Even over surface
C1	11	100% Surface	Occasional Thin Spots
D1	3	100% Surface	Occasional Thin Spots

*Tear Break-up Time (seconds)

The polymer complex (B1 and C1) of the cationic cellulosic polymer and PEO provides an adsorbed layer on the contact lens surface which is compatible with the tear film and supports long tear break up time.

EXAMPLE 3

The solutions in Tables 3 and 4 were prepared as in Examp1 1, and dynamic contact angles (DCA) were

determined on wafers of the RGP for the various solutions described in TABLE 1. The DCA results are summarized in TABLE 5.

Additionally, the rates of adsorption were qualitatively determined by analyzing each of the seven individual dip cycles into the test solution. The rate of desorption was then determined by dipping a coated wafer into non-preserved phosphate buffer for 14 cycles. The measured advancing angle was utilized in both cases as a measure of absorbed polymer complex on the test material surface. In TABLE 5, the designation "mod." denotes "moderate".

TABLE 3

	Solution		
	E	F	G
Sodium Phosphate, dibasic %	0.280	0.280	0.280
Potassium Phosphate, monobasic %	0.055	0.055	0.055
Sodium Chloride %	0.700	0.700	0.700
Potassium Chloride %	0.050	0.050	0.050
Disodium Edetate %	0.050	0.050	0.050
UCARE Polymer JR-30M %	0.002	0.0018	0.0016
POLYOX WSR N-10 %	0	0.0002	0.0004
Deionized Water Q.S. %	100	100	100

TABLE 4Solution

	H	I	J
Sodium Phosphate, dibasic %	0.280	0.280	0.280
Potassium Phosphate, monobasic %	0.055	0.055	0.055
Sodium Chloride %	0.700	0.700	0.700
Potassium Chloride %	0.050	0.050	0.050
Disodium Edetate %	0.050	0.050	0.050
UCARE Polymer JR-30M %	0.0014	0.001	0
POLYOX WSR N-10 %	0.0006	0.001	0.002
Deionized Water Q.S. %	100	100	100

TABLE 5

<u>Solution</u>	E	F	G	H	I	J
Adv (Abs)	34	85	35-80	22-80	30-80	25-85
Adsorption	very strong	weak	mod. strong	mod. strong	mod.	weak
Adv (Des)	25-70	84	83	83	89	96
Desorption	slow	fast	fast	fast	very fast	very fast

Adv. (Abs) Advancing contact angle in degrees for absorption

Adv. (Des) Advancing contact angle in degrees for desorption

We claim:

1. An aqueous solution for treating contact lenses comprises a cationic cellulose polymer and polyethylene oxide.

2. The composition of claim 1, wherein the cationic cellulosic polymer is selected from the group consisting of a cellulosic polymer containing N,N-dimethyl amino ethyl groups and a cellulosic polymer containing N,N-dimethyl amino-2-hydroxypropyl groups.

3. The composition of claim 1, wherein the cationic cellulosic polymer is a cellulosic polymer containing quaternized N,N-dimethyl amino groups along the cellulose polymer chain.

4. The composition of claim 1 further comprising an antimicrobial agent.

5. The composition of claim 1 further comprising a wetting agent.

6. The composition of claim 1 further comprising a buffering agent.

7. The composition of claim 1 further comprising a tonicity adjusting agent.

8. A method of treating a contact lens comprising contacting said contact lens with an aqueous composition which comprises a cationic cellulose polymer and polyethylene oxide.

9. The method of claim 8, wherein the cationic cellulosic polymer is selected from the group consisting of a cellulosic polymer containing N,N-dimethyl amino ethyl groups and a cellulosic polymer containing N,N-dimethyl amino-2-hydroxylpropyl groups.

10. The method of claim 8, wherein the cationic cellulosic polymer is a cellulosic polymer containing quaternized N,N-dimethyl amino groups along the cellulose polymer chain.

11. The method of claim 8, wherein the composition further comprises at least one member selected from the group consisting of buffering agents and tonicity adjusting agents.

12. A method of disinfecting and wetting a contact lens comprising contacting said contact lens with an aqueous composition which comprises a cationic

cellulosic polymer, PEO, and an antimicrobially effective amount of an antimicrobial agent.

13. The method of claim 12, wherein the cationic cellulosic polymer is selected from the group consisting of a cellulosic polymer containing N,N-dimethyl amino ethyl groups and a cellulosic polymer containing N,N-dimethyl amino-2-hydroxylpropyl groups.

14. The method of claim 12, wherein the cationic cellulosic polymer is a cellulosic polymer containing quaternized N,N-dimethyl amino groups along the cellulose polymer chain.

15. The method of claim 12, wherein the composition further comprises at least one member selected from the group consisting of buffering agents and tonicity adjusting agents.

INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 C11D3/00 C11D3/22 C11D3/37 G02C13/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 5 C11D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US,A,4 321 261 (ELLIS ET AL.) 23 March 1982 cited in the application see column 4, line 18 - line 27 see column 7, line 23 - line 68 see claims	1-15
A	& US,A,4 168 112 (ELLIS ET AL.) 18 September 1979 cited in the application	
A	& US,A,4 436 730 (ELLIS ET AL.) 13 March 1984	1-15
A	GB,A,1 340 516 (BURTON PARSONS CHEMICALS INC.) 12 December 1973 see claims 1-8,13,19-23	1,4-6,8, 12,15
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☒ Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PATENT ABSTRACTS OF JAPAN vol. 013, no. 426 (P-935) 22 September 1989 & JP,A,01 158 412 (DAICEL CHEM IND LTD) 21 June 1989 see abstract ---	1-8
A	DATABASE WPI Section Ch, Week 8914, Derwent Publications Ltd., London, GB; Class A96, AN 89-103364 & JP,A,1 050 014 (TOME SANGYO KK) 27 February 1989 see abstract -----	1-8

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